III. REMARKS

Claim Status

Claims 1, 3-15 and 17-20 are in the case. Claims 1, 3-8, 10-15, and 17-20 have been amended. Claims 21 and 22 are new.

Objections

The disclosure is objected to because the specification contains too many grammatical, idiomatic, and spelling errors to list specifically and should be carefully revised.

Applicant has reviewed the specification and run a spell check and does not find the number of grammatical, idiomatic, and spelling errors indicated by the examiner. Applicant is willing to amend those errors identified by the examiner.

The Invention

The invention is directed to solving a problem associated with elastase 1-ELISA tests. Applicants have determined that current elastase 1-ELISA tests result in numerous false negative results. [spec. page 2]. Applicants have further determined that these false negative results are the result of the failure of current tests to recognize that elastase exists in various iso-forms and further, in the inability of current tests to react to all the various isoforms.

Thus, applicant was first to recognize a problem with current tests. Having recognized the problem, applicants endeavored to solve the problem. They were successful in doing so.

The novel procedure developed by applicants utilizes antibodies in the same manner as existing tests but raises those antibodies by exposure to specific antigens which "used either singly or in combination represent all known elastase iso-enzymes or partial elements of such enzymes or cross-reacting synthetic sequences." [spec. page 3, 2nd paragraph].

Until the problem was recognized, one skilled in the art would not know how to solve the problem, so applicant's solution is inherently unobvious. It is only with hindsight knowledge of the cause of the problem that one skilled in the art would be motivated to solve the problem by developing novel test procedures.

In the present case applicants disclose a procedure for producing anti-elastase antibodies "in the usual way." [spec. page 3].

It is also clear that the procedure for utilizing the antibodies and the test procedures for the presence of elastase are unchanged and no additional disclosure of such current practices is required.

So the point of novelty [or lack thereof] is based on the provision of antibodies to all known elastase iso-enzymes as stated in applicant's specification.

Claims Rejections - 35 U.S.C. 112, first paragraph

Claims 1, 3-11 and 17-20 stand rejected under 35 U.S.C. 112, first paragraph, for the reason that the specification contains subject matter which was not described in such a way as

to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, and which was not described in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicant traverses this ground for rejection.

First, as applicant identifies in his specification, at page 2, elastase 1 tests were known and used in the art at the time of his invention. At page 2, third paragraph, applicant identifies a problem with the then existing test, i.e. the traditional elastase-1 ELISA test is not sufficiently sensitive to recognize pancreas elastases.

Inherently then, those skilled in the art did not need to be taught the procedure for determining elastase-1 at the time this invention was made, nor that the detection of elastases had diagnostic significance.

Applicant determined that the elastase protein existed as various iso-enzymes and conceived of a method utilizing the various iso-enzymes to increase the sensitivity of the test. As stated on page 3, lines 17-19,

> "The invention therefore relates to a procedure for producing anti-elastic antibodies in the usual way." [emphasis supplied]

The novelty is specified in the next sentence:

> "… the specific antigens used either single or in combination represent all known elastases iso-enzymes or partial elements of such enzymes or cross-reacting synthetic sequences."

So what is claimed is 1) a method of producing samples containing various elastases, 2) collecting the various iso-forms, 3) raising antibodies to the collected iso-forms and 2) using the set of antibodies so collected in tests thereby increasing the sensitivity of the test.

Applicant suggests that each of the steps above comprises a procedure known in the art and that the statement of the step is sufficient and that once the inventive step of using multiple iso-forms is stated the remaining necessary information is contained in the specification and was known to the art and contained in the references cited hereinbelow.

Claims 1, 3-11 and 17-20 stand rejected under 35 U.S.C. 112, first paragraph, for reasons of record, that the specification contains subject matter which was not described in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, and which was not described in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicant urges that elastase assay reagents and steps were known to the art.

The examiner reiterates that applicant teaches only polyclonal antibodies and provides no description or guidance to any monospecific species which functions in the invention.

Applicant traverses this ground for rejection and cites the specification, at page 3, last sentence as basis for monoclonal as well as polyclonal antibodies.

The examiner further states that adequate written description requires more than a mere statement that a product is part of the invention, more than a reference to a potential method of isolating it, and more than a generic statement which defines a genus of products by only their functional activity. and that the product itself is required as well as recitation of a representative number of products falling within the scope of a claimed genus.

Applicant notes that the claims are method claims and claim a novel procedure for using known or readily produced products. Applicants expressly stated in his specification that the products are not claimed as novel, the process of using non-novel products is what is being claimed.

The examiner also states that all possible analogs of a product are not enabled by a disclosure wherein the characteristics of the analogs are unpredictable. Again, the analogs are not being claimed, merely the use of analogs that are functional in the novel method. The characteristic of the analog is specified in the specification and claims - that it be functional in the claimed process for determining isoforms of pancreatic elastases.

Applicant reiterates that it is the process that is novel, not the products used in the process.

The examiner states that, "there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art", "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement." [emphasis supplied]

The examiner's statement of the applicable law is correct but begs the question. The question is what the point of novelty is.

The point of novelty is the provision of specific antigens that recognize all elastase iso-enzymes. As discussed above, this is disclosed in the specification (page 3, 2nd paragraph) and thus the novel aspects of the invention are expressed in the specification. These specific antigens are preferably obtained by peptide synthesis (page 3, 3rd paragraph)

The knowledge required to produce these peptides is not novel and is possessed by one skilled in the art. The examiner states that absent further written description and guidance from applicant, one would have no assurance of successfully obtaining appropriate functional reagents and predictably performing the method as suggested by applicant. Applicant traverses this ground for rejection in that applicant has disclosed and claimed 15 specific peptides [claim 17] that fulfill the claimed function.

The examiner argues that applicant also provides no guidance for usable combinations, particularly since some of the peptides suggested for use by applicant would be expected to elicit antibodies that bind to an isoform that corresponds to porcine elastase, which is not expressed in the human pancreas, and which would complicate the assay in certain patient populations.

Assuming, *arguendo*, that, as stated by the examiner, the assay would be complicated in certain patient populations, this nonetheless is no basis for rejection of applicant's claims. This is further confirmed by the document submitted herewith entitles "Detection of pancreatic Elastases 3A and 3B by a polyclonal Elastase ELISA" which demonstrates that where there is a cross reactivity, the antisera can easily be removed from the system.

Further, for reasons of record, the examiner argues that applicant does not teach combinations usable together and that one could not predict the ability of any of the antibodies to the suggested peptides to bind to non-denatured protein as found in a fluid sample from a patient for the reasons of record.

Applicant does not rely on mere attorney argument to demonstrate the usability of the instant invention. Applicant provided, with his last response ten [10] technical publications demonstrating the suitability and practicability of the claimed method.

These technical publications are, in combination with the two new references submitted herewith, more than sufficient to overcome any *prima facie* case the examiner has made out and

therefore requests favorable reconsideration of this ground for rejection.

Claim Rejections – 35 U.S.C. § 112, second paragraph

Claims 1, 3-15, and 17-20 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 3-5, and 20 are method claims and stand rejected for using "employing" or "using" as not being valid method steps.

Applicant notes that the offending terms are not present in claim 1.

The other claims have been amended to remove the offending terms.

In addition, in these claims, "the antigen" lacks antecedent basis. Applicant notes tht the offending term is not present in claims 5 or 20.

In claims 3-4, improper Markush language is used to claim the members of the group.

The claims have been amended to obviate this ground for rejection.

In claim 6, "the pancreas" lacks antecedent basis and it is not clear what applicant intends as excluded because the excluded amino acid sequence is of a peptide not an iso-enzyme.

Claim 6 has been amended to obviate this ground for

rejection.

In claim 7 and claims dependent thereupon, incorrect "SEQ ID NO:" identifiers are recited and it is not clear what is intended as encompassed by "such" peptides or antibodies, i.e. are the elements merely exemplary of what is within the metes and bounds of the desired invention or is the invention limited to only those elements specifically recited.

Applicant has amended claim 7 to identify the correct sequence identifies and to delete the word “such” thus obviating this ground for rejection.

In claim 8, it is not clear how one determines what is "suitable" and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

“Suitable” has been deleted from the claim to obviate this ground for rejection.

Claims 10 and 11 are rejected as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Applicant traverses this ground for rejection. Claims 10 and 11 depend on claim 7 which claims both mono and polyclonal antibodies. These claims further limit claim 7 by claiming only 1 of the 2 types of antibodies claimed in claim 7.

Claims 12-15 each fails to end with a period.

A period has been added to obviate this ground for rejection.

Claims 17 and 18 are rejected as indefinite in that the claims fail to further limit the subject matter of a previous claim and set forth an intended use but fail to point out what components are included or excluded by the claim language and, in these claims, "the diagnosis" lacks antecedent basis.

Claim 17 has been amended to obviate this ground for rejection.

In claim 19, it is not clear what step of claim 7, if any, is being further limited.

The examiner correctly surmises that applicant intended the subject matter of the claim to depend from claim 8. This claim has now been amended to correct the typo.

In claim 20, it is not clear what step of claim 3, if any, is being further limited because "the induction of B-cells" lacks antecedent basis. It is not clear what is intended by "hybridoma cells which are cultivated in cell lines."

Claim 20 has been cancelled.

Claim Rejections - 35 U.S.C. § 102(b)

Claims 1, 3-8, 10-15, and 17-20 are rejected under 35 U.S.C. § 102(b) as being anticipated by Scheefers et al. (USP 5,622,837) in light of the instant disclosure for reasons of record.

Claims 1, 3-8, 10, 12-15, 17 and 18 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Sziegoleit et al. (Clin. Biochem. 22: 79, 1989) in light of the instant disclosure for

reasons of record.

Applicant traverses these grounds for rejection.

Sziegoleit et al. discloses a method for the detection of elevated elastase 1 levels in the serum of patients. Scheefers et al. discloses a method for obtaining highly specific elastase 1 antibodies for diagnosis and monitoring pancreatitis.

Both documents describe only the detection of elastase 1. In contrast present invention describes a method for detecting all known elastase isoenzymes. Further, antibodies of present invention are specific for more and different parts of amino acid sequences of those isoenzymes. Elastase enzymes are digested when they reach the intestinal tract. The antibodies described in Scheefers et al. are unable in many cases to bind to the snatches of the digested enzyme, because they are only specific for a single amino acid sequence.

It was an unexpected result that antibodies of present invention are able to detect even those snatches of digested elastase isoforms.

That leads to an advantage of the present invention over the prior art.

Sziegoleit is only useable in serum, Scheefers et al. is not as effective as present invention by detecting elastase in stool. Furthermore, both documents describe only detection of elastase 1 and not the detection of further isoenzymes as possible by using the invention of present patent application.

The examiner states that, notwithstanding applicant's

assertions to the contrary, Scheefers et al. clearly teach elicitation of both polyclonal and monoclonal antibodies to purified enzyme, not only to the peptide disclosed in the reference. And, as is noted by applicant, the excluded sequence is not found in the purified enzyme.

The examiner argues that the enzyme isolated from multiple organs by the references of Sziegoleit et al. or Scheefers et al. would inherently be a mixture of the elastase I isoforms (i.e. elastases IIIA and IIIB), and polyclonal antibodies elicited thereto would inherently bind to the isoforms and cross-react with similar epitopes as found in elastase II.

The examiner correctly points out that the Patent and Trademark Office does not have the facilities and resources to provide the *factual* evidence needed in order to establish that there is a difference, in the first place, between the reagents of the prior art and those instantly disclosed and, that if there is such a difference, that such a difference would have been considered unexpected by one of ordinary skill in the art.

The examiner states that the burden is upon applicant to present such factual evidence.

Applicant previously presented numerous references demonstrating the lack of inherency of the prior art compositions to detect all isoforms.

Applicant encloses with this response a further reference, entitled "Assessment of Isoforms specificity for a polyclonal Elastase ELISA". The paper describes a test procedure using three different polyclonal antisera that are used in commercial ELISA

tests for the presence of elastase. The results demonstrate that all three antisera identified isoforms IIIA and IIIB but not isoforms II or I.

The failure of these three different polyclonal antisera used in a commercial ELISA test to identify all isoforms demonstrates that the prior art would not necessarily be a mixture of all isoforms.

The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993). "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.' " *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999).

"In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original)

Thus, the doctrine of inherency does not apply and the examiner has not made out a *prima facie* case.

For the forgoing reasons, applicant believes the references do not explicitly or inherently read on applicant's claims. Favorable reconsideration is respectfully requested.

The Commissioner is hereby authorized to charge payment for any fees associated with this communication or credit any over payment to Deposit Account No. 14-1263.

Respectfully submitted,

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